

Frans J. Kok
Daan Kromhout

Atherosclerosis

Epidemiological studies on the health effects of a Mediterranean diet

■ **Summary** Mediterranean diets are characterized by olive oil, as the dominant fat source and a high to moderate consumption of fruit and vegetables, cereal products, fish, legumes, in combination with little meat and wine with meals.

The 'reference' Mediterranean diet seems to differ according to country, but is associated with

good health and a long life expectancy. From the Seven Countries Studies, it has been shown that especially the traditional Cretan diet was associated with very low 25-year mortality rates for coronary heart disease, cancer and all-causes.

In terms of nutrients and bioactive compounds the 'reference' Mediterranean diet is low in saturated fat and high in monounsaturated fatty acids, high in antioxidants especially vitamin C and E, and high in fiber and folic acid. Several epidemiological studies have investigated these dietary components either separately or in combination in other than Mediterranean populations. In general, also in other populations beneficial effects on the coronary risk profile have been observed, which

gives further support to the positive health effects of the Mediterranean diet.

Intervention studies in East Finland and Southern Italy have convincingly shown that the coronary risk profile (lower LDL cholesterol and blood pressure levels) is improved by a Mediterranean diet. Moreover, the Cretan diet was tested in cardiac patients and showed a 70 % lower cardiac and all-causes mortality compared to the control diet.

In conclusion, epidemiological studies and intervention trials suggest that the Cretan Mediterranean diet lowers the risk of coronary heart disease.

■ **Key words** atherosclerosis – mediterranean diet – CHD

Professor Frans J. Kok (✉)
Wageningen University
Division of Human Nutrition
& Epidemiology
P.O. Box 8129
6700 EV Wageningen, The Netherlands
E-Mail: frans.kok@wur.nl

Daan Kromhout
Division of Nutrition and Consumer Safety
National Institute of Public Health
& The Environment
Bilthoven, The Netherlands

The Mediterranean diet

The original Mediterranean diet can be defined as the dietary pattern found in the olive-growing areas of the Mediterranean region in the late 1950s and early 1960s [1]. The Mediterranean Sea borders 18 countries and the diets vary from country to country. For example, the Italian Mediterranean diet is moderate in olive oil and high in cereals, the Greek diet uses much more olive oil and fruits and in Spain olive oil and fish are popular foods.

Although there are several variants of the Mediterranean diet, some common components can be identi-

fied: low saturated fat, high monounsaturated fat; moderate intake of alcohol, mainly in the form of wine with meals; high consumption of vegetables, fruits, legumes, and cereals; moderate consumption of fish, milk and dairy products, mostly in the form of cheese; and low consumption of meat and meat products [1].

This review focuses on the Greek variant of the Mediterranean diet, for reasons that are no better than the fact that Greeks have been in the area longer than most other people and because the first studies that showed beneficial effects of the Mediterranean diet, were largely based in Greece.

Dietary composition

The report of the Rockefeller Foundation describing the Cretan diet in 1948 concluded that “olives, cereal grains, pulses, wild greens and herbs, and fruits, together with limited quantities of goat meat and milk, game and fish have remained the basic Cretan foods for 40 centuries . . . , no meal was complete without bread . . . Olives and olive oil contributed heavily to the energy intake . . . food seemed to be “swimming” in oil” [2].

In the 1960s the Cretan diet was still rich in bread and cereals, legumes, fruit, and vegetables, high in edible fats mostly olive oil. It contained much less meat and supplied moderate amounts of fish and alcohol, mostly in the form of wine (Tables 1 and 2) [3]. In contrast, in the United States the consumption of fruit, meat, and pastries was high. The northern European diet was generally characterized by a high consumption of potatoes, milk, butter or margarine, and sugar products.

Detailed analysis of the type and amounts of visible fats consumed showed a very high average intake of butter in Finland (about 75 g per day, data not shown) and intermediate amounts in the United States and The

Netherlands (Zutphen cohort) (about 20 g per day; Table 2). Olive oil consumption was very high in Crete (95 g per day).

Fatty acids

The average total fat content of the Cretan diet in 1960 was 40 % energy (Table 3). In spite of the high fat content the intake of saturated fatty acids was less than 10 % of energy. A high average total and saturated fatty acid intake was found in Zutphen (44 and 20 % E, respectively). In the Mediterranean diets trans fatty acids were almost non-existent, but the diet of the Zutphen men contained about 8 g per day. A very high intake of monounsaturated fatty acids was observed in Crete, about 80 g per day compared with about 50 g per day in Zutphen.

The average intake of saturated, monounsaturated fatty acids and N-6 polyunsaturated fatty acids by middle-aged Cretan men in 1960 is well documented. The estimate of N-3 polyunsaturated fatty acids and especially of α -linolenic acid can be questioned. The average intake of α -linolenic acid was 1.2 g per day in 1960, compared with 2.2 g per day in the Zutphen cohort of the Seven Countries Study [4]. In a comparative study in elderly men from Zutphen and Crete carried out in the 1980s, the average concentration of α -linolenic acid in the cholesteryl esters was three times higher in Crete compared with Zutphen (0.9 vs. 0.3 %) [5]. The other characteristic difference in the fatty acid composition of the Cretan and Zutphen diet, as a high intake of oleic acid in Crete and a high intake of linoleic acid in Zutphen were reflected in the fatty acid composition of the cholesteryl esters. It is therefore likely that the intake of α -linolenic acid in the Cretan diet of 1960 was underestimated because information about the consumption of wild greens like purslane, commonly present in Cretan

Table 1 Average amount of vegetable and animal foods consumed per person in g per day in 1960: selected cohorts of the Seven Countries Study

Cohort	Bread	Cereals	Potatoes	Legumes	Vegetables	Fruit
U. S. railroad	97	26	124	1	171	233
Zutphen	252	17	252	2	227	82
Crete	380	30	190	30	191	464

Cohort	Meat	Fish	Eggs	Cheese	Milk
U. S. railroad	273	3	40	18	231
Zutphen	138	12	27	31	447
Crete	35	18	25	13	235

Table 2 Average amount of visible fats and other foods consumed per person in g per day in 1960: selected cohorts of the Seven Countries Study

Cohort	Butter	Margarine	Lard	Olive oil	Other
U. S. railroad	26	4			3 ^a
Zutphen	21	56	2		
Crete				95	

Cohort	Edible fats	Sugar products	Pastries	Alcohol 100%	Rest
U. S. railroad	33	24	95	6	91
Zutphen	79	72	29	3	29
Crete	95	20	0	15	107

^a soy bean oil

Table 3 Population average dietary fatty acid and antioxidant intake in Crete and Zutphen cohorts in 1960

Cohort	Fatty acids				
	Total (%E)	SFA (g)	TFA (g)	MUFA (g)	PUFA (g)
Crete	40.1	28.0	0.4	84.1	13.4
Zutphen	43.7	60.9	8.1	49.5	20.7

Antioxidants (mg)				
	β -carotene	Vitamin E	Vitamin C	Flavonoids
Crete	1.8	23.3	136	15.7
Zutphen	2.9	11.6	110	33.1

SFA Saturated Fatty Acids; TFA Trans Fatty Acids; MUFA Mono Unsaturated Fatty Acids; PUFA Poly Unsaturated Fatty Acids

salads and an important source of α -linolenic acid, was not available.

■ Antioxidants

In the Seven Countries Study, vitamin E intake was high (about 23 mg per day, Table 3) in Crete and low in the Japanese cohorts (about 8 mg per day, not shown). The United States and the Greek cohorts had the highest intake of vitamin C (about 135 mg per day). The intake of flavonoids was highest in Japan (about 65 mg per day) and lowest in Finland (about 5 mg per day) [6]. The average intake of flavonoids in the Cretan cohorts was relatively low (15.7 mg/day, Table 3). This could be due to underestimation because the flavonoid content of wild greens was not known at that time.

Wild greens are an important sources of antioxidants, especially flavonoids. In 1997 the flavonoid content of six major flavonoids, including quercetin, were analyzed in seven different wild greens [7]. The quercetin content varied per 100 g wild greens from 1.1 to 86.2 mg, and was very high in fennel (46.8 mg) and Queen Anne's lace (86.2 mg). These concentrations are higher than in onions (34.4 mg), a vegetable known for its high flavonoid content. These results show that wild greens are rich sources of flavonoids. In 1960 no information was available about the consumption of wild greens. It is therefore likely that the average flavonoid intake of the middle-aged Cretan men in 1960 was underestimated.

Finally, olive oil is rich in phenols, antioxidants which may decrease LDL oxidisability and thus lower the risk for atherosclerotic complications.

Observational epidemiology

Interest in the Mediterranean diet derives from results in the Seven Countries Study. Keys et al. who demonstrated that the mortality rate from coronary heart disease (CHD) after 5–15 years follow-up in southern Europe was two- to threefold lower than in northern Europe or the United States [8]. In that study, the mortality from CHD and all-causes in the cohort from Crete was much lower than that among the nine other cohorts from southern Europe.

Also after 25 years, the lowest mortality rates for CHD, cancer and all-causes were found in Crete (Table 4). The mortality rate for CHD was four times higher, for cancer twice as high, and for all-causes, 50 % higher in Zutphen compared to Crete [3].

These observations suggest that the population of Crete could be considered to have the best life expectancy in the Western world, even though average serum cholesterol concentrations in the Cretan popula-

Table 4 Total and cause-specific 25-year mortality rates in the Crete and Zutphen cohorts of the Seven Countries Study

	25-year mortality rate (%)		
	CHD	Cancer	All-causes
Crete	4.6	8.8	31.4
Zutphen	19.7	17.8	48.0

tion were similar to those in the other Mediterranean cohorts [8].

Trial evidence

■ Coronary risk profile

The positive health effects of the Mediterranean diet on CHD risk factors has been tested in intervention studies carried out in eastern Finland and southern Italy. Middle-aged men and women changed their usual Finnish diet for six weeks to a Mediterranean type of diet [9]. This change in diet was associated with a more than 20 % decrease in total and LDL cholesterol and apoprotein B. A similar study showed a significant blood pressure lowering effect of such a change in diet [10]. At about the same time a study was carried out in southern Italy investigating the effect of a change from a traditional Mediterranean diet to a diet higher in saturated fatty acids, and cholesterol [11]. These dietary changes were associated with an increase of 15 % in total cholesterol and 19 % in LDL cholesterol. Replacing dietary saturated fatty acids with monounsaturated oleic acid from olive oil decreases plasma LDL concentrations [12]. The available evidence does not suggest that consumption of phenols in the amounts provided by dietary olive oil will protect LDL against oxidative modification to any important extent [13].

These results show convincingly that a Mediterranean type of diet improves the levels of major CHD risk factors, such as LDL cholesterol, and blood pressure.

■ Coronary and all-cause mortality

In Lyon, France, Renaud et al. have tested the hypothesis that an α -linolenic acid enriched Cretan Mediterranean diet, as consumed in the early 1960s, would more effectively protect against CHD than the prudent diet that is often recommended for coronary patients. For the trial 605 cardiac patients were randomized and followed for 27 months [14]. The effect on coronary and all-causes mortality of the Cretan Mediterranean diet adapted to a Western population was compared with a usual prescribed diet. Both diets had a moderate amount of total

fat (31–33 % of energy) and saturated fatty acids (8.3 % of energy in the experimental group and 11.8 % of energy in the control group). The largest difference was in α -linolenic acid (1.8 g per day in the experimental group and 0.79 g per day in the control group). The experimental group also had a higher consumption of fruits and vegetables, as reflected in the higher intake of vitamin C. These differences in diet were associated with a 70 % lower cardiac and all-causes mortality in the experimental compared with the control group.

From results of this trial it was concluded that a diet adapted from the Cretan Mediterranean diet was much more efficient in preventing (sudden) cardiac death and total death than the diet high in linoleic acid that is usually prescribed by cardiologists for coronary patients [8]. The specific factors that contribute to the protective effects of this diet need further investigation, but the low intake of saturated fatty acids (8 % of energy), the high concentrations of oleic acid, the 1:5 ratio of 18:3n-3 (α -linolenic acid) to 18:2n-6 (linoleic acid), and the high concentrations of natural antioxidants seem to be the most reasonable candidates. The moderate intake of meat and of wine could also contribute to the protective effects. The findings that serum lipids (total, LDL, and

HDL cholesterol) were similar in the experimental and control groups, that protective effects were observed within a few months, and that similar results have been obtained with an increased intake of fish, suggest that the mechanism may involve a direct effect on thrombogenesis [8]. No sudden death occurred in the experimental group which suggest antiarrhythmic effects of the Cretan Mediterranean diet.

Conclusions

Evidence is accumulating on the positive health effects of Mediterranean diets. Most evidence is available for the Cretan Mediterranean diet. Observational and experimental data suggest that a Cretan Mediterranean diet characterized by a high consumption of olive oil, fruits, vegetables, cereals and legumes and a moderate consumption of fish and wine with meals was associated with low rates of coronary and all-cause mortality. This traditional Mediterranean diet is a more attractive approach to healthy eating than are the low-fat, dietary modification of Western food products and cuisine.

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